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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,024	JONES ET AL.	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 5/10/06.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) 24-29 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 10 November 2004 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11/10/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims:

Applicants' election, with traverse, of Group I, claims 1-21, directed to nucleic acids, filed on 10 May 2005 in response to the Requirement for Restriction of 29 March 2006 is acknowledged. The traversal is on the grounds that the restriction requirement is too narrowly drawn and that in particular, Group II, drawn to proteins, should be rejoined with Group I. Upon further consideration, Applicants arguments have been found to be persuasive. Group I will be rejoined with Group II and claims 1-23 will be examined together. The restriction between these two groups and Groups III and IV remains. In response to requirement for species election, applicants have elected specie A, with traverse. The traversal is on the grounds that the election of species is too narrowly drawn, since the examination of sequences that differ in respect to only one to three nucleotides is not an undue burden. Applicants' arguments have been found to be persuasive and the requirement for a species election is withdrawn.

Claims 1-29 are pending in the instant application. Claims 24-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-23, drawn to isolated nucleic acids and encoded proteins, are under examination.

Objections

Figures and/or Drawings

Figure 1A is objected to because SEQ ID NO:14 is not identified as DR-4, as disclosed in "Brief Description of the Drawings" on page 8, lines 21-28.

Figure 3B and C is objected to because the brief description of the drawings indicates objects in color, but the drawings in the patent application are in black and white.

Figure 4C is objected to because the brief description refers to open circles, hashed circles and filled circles, but only the filled circles are present in the figure.

Figure 6A is objected to because the brief description of the drawings indicates objects in color, but the drawings in the patent application are in black and white.

Figures 7 and 8 are objected to because tables and sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Appropriate correction is required. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Applicants should amend the specification to delete any Figures which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO:.

Appropriate correction is required.

Claim Rejections

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C., second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-21 recite "An isolated nucleic acid capable of hybridizing to SEQ ID NO:1 under stringent conditions..." The specification discloses "stringent conditions involve hybridizing .....The parameters of salt concentration and temperature [may] be varied to achieve optimal level of identity..." (page 23, lines 16-20). Thus, the definition of stringent conditions in the specification is non-limiting. The claims are therefore vague and indefinite.

Claim 7 is vague and indefinite in that it does not recite a claim to a particular subject matter.

Claims 6 and 12 recite an isolated nucleic acid encoding the same USP variant protein; Claims 8 and 13 recite an isolated nucleic acid encoding the same USP variant protein; Claims 9 and 14 recite an isolated nucleic acid encoding the same USP variant protein; Claims 11 and 15 recite an isolated nucleic acid reciting the same USP variant protein. Claims 6, 8, 9 and 11 all recite the limitation "which upon binding an epoxy farnesoid-like ligand results in transcriptional activation of a nuclear hormone receptor reporter construct". Claims 12-15 all recite the limitation "which has dominant negative nuclear hormone receptor activity". The specification defines a protein that acts as a "dominant negative" as a mutant protein the "homodimerizes or heterodimerizes with an endogenous wild type partner to form a complex following ligand or independent of ligand binding. Preferably, as opposed to a complex of wild type monomers, a complex of a mutant and its endogenous wild type partner will be incapable of initiating transcription [at] a hormone receptor response reporter gene" (page 15, lines 9-19). It is unclear how the identical variant protein can activate a nuclear hormone receptor reporter construct and can be incapable of initiating transcription of a hormone receptor response reporter gene. Therefore, the metes and bounds of the claim cannot be determined.

Claims 22 and 23 are indefinite because Claims 22 and 23 comprise improper Markush groups; these claims recite "the protein of any of claims 1 to 11" or "the protein of any of claims 12 to 21". So the protein could be from one, two or all of the claims. Multiple dependent claims must refer to the claims from which they depend in the alternative only, not inclusively. It is suggested the claims be rewritten as: " A protein

comprising the protein sequence in any one of claims 1 to 11" and "A protein comprising the protein sequence in any one of claims 12-21". See M.P.E.P. 608.01(n) for acceptable multiple dependent claim wording.

Claims 1-21 are drawn to nucleic acid molecules and the variant proteins these nucleic acid molecules encode. The nucleic acid of SEQ ID NO:1 encodes the polypeptide of SEQ ID NO:2, the Ultraspiracle protein which is well known in the art (see, for example, 1990. Oro et al. Nature 347:298-301).

It is suggested the claims (1-21) be rewritten as, for example: "An isolated nucleic acid encoding a protein of SEQ ID NO:2 having a X residue in a first position corresponding to position Y of SEQ ID NO:2 and an A residue in a second position corresponding to position B of SEQ ID NO:2 which activates transcription of a nuclear hormone receptor reporter construct upon binding an epoxy farnesoid-like ligand".

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 8, 9 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When

determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 6 and 12 are both drawn to an isolated nucleic acid encoding a protein having a tryptophan residue in a first position corresponding to position 477 of SEQ ID NO:2 and a tryptophan residue in a second position corresponding to position 479 of SEQ ID NO:2. Claims 8 and 13 are both drawn to an isolated nucleic acid encoding a protein having a phenylalanine residue in a first position corresponding to position 318 of SEQ ID NO:2, and a phenylalanine residue in a second position corresponding to position 328 of SEQ ID NO:2. Claims 9 and 14 are both drawn to an isolated nucleic acid encoding a protein having a tryptophan residue in a first position corresponding to position 498 of SEQ ID NO:2, a tryptophan residue in a second position corresponding to position 499 of SEQ ID NO;2 and a phenylalanine residue in a third position corresponding to position 318 of SEQ ID NO:2. Claims 11 and 15 recite an isolated nucleic acid encoding a protein having a tryptophan residue in a first position corresponding to position 498 of SEQ ID NO:2, a tryptophan residue in a second position corresponding to position 499 of SEQ ID NO:2, a phenylalanine residue in a third position corresponding to position 318 of SEQ ID NO:2, a phenylalanine in a fourth position corresponding to position 328 of SEQ ID NO:2.

Claims 6, 8, 9 and 11 all recite the limitation "which upon binding an epoxy farnesoid-like ligand results in transcriptional activation of a nuclear hormone receptor reporter construct". Claims 12-15 all recite the limitation "which has dominant negative nuclear hormone receptor activity".

The specification discloses the following definitions:

"Transcriptional activity" of a protein or nuclear hormone receptor .....refers to the ability of a nuclear hormone receptor to homo- to heterodimerize, bind a nuclear hormone receptor response element and induce the transcription of any nucleic acid operably linked thereto", ie. reporter construct (page 13, lines 20-24).

Dominant negative protein[s] .....forms a dimer with an integral part of a wild type endogenous protein molecule..... the mutant protein the homodimerizes or heterodimerizes with an endogenous wild type partner to form a complex following ligand or independent of ligand binding. Preferably, as opposed to a complex of wild type monomers, a complex of a mutant and its endogenous wild type partner will be incapable of initiating transcription [at] a hormone receptor response reporter gene" (page 15, lines 9-19).

The specification goes on to teach the mutant nuclear hormone receptors have both altered fluorescent properties upon ligand binding as well as dominant negative activity (page 15, lines 21-22). Table I indicates that some of these mutant proteins exhibit altered fluorescence with respect to the wild type and weak dominant negative activity. However, the definition of weak dominant negative activity is not disclosed in the specification. Thus, the claims encompass identical proteins that exhibit two conflicting characteristics: a protein capable of activation of transcription of reporter gene, and a protein incapable of initiating transcription of a reporter gene. The specification does not teach one of ordinary skill in the art how to make a single protein which exhibits both of these conflicting activities.

Due to the large quantity of experimentation necessary to generate a polypeptide encompassed by the claims of the instant invention, the lack of direction/guidance presented in the specification as to how to generate a polypeptide that maintains two contradictory biological properties, the absence of working examples directed to same, the complex nature of the invention, the state of the art which teaches that a protein's properties are ultimately dependent upon its primary structure, and thus a single protein sequence cannot exhibit conflicting activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Prior art made of record:

The following prior art is made of record and not relied upon is considered pertinent to applicant's disclosure. Oro et al. (1990, Nature 347:298-301, Figure 2) and Venter et al. (2001, WO 01/71042 A3, SEQ ID NO:17156 and SEQ ID NO:8580) disclose sequences that are 100% identical with SEQ ID NO:1 (nucleic acid) and SEQ ID NO:2 (protein) disclosed in the instant invention. However neither of the references teach or suggest the variant protein sequences disclosed in the instant invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

Lorraine Spector

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PRIMARY EXAMINER